Ciliary neurotrophic factor

Schwann cells play an important role in not only producing neurotrophic factors such as nerve growth factor (NGF) and ciliary neurotrophic factor (CNTF), which promote growth, of both the damaged nerve and supporting Schwann cells, but also producing neurite promoting factors, which guide the growing axon.

Ciliary neurotrophic factor receptor α subunit (CNTFRα) and CNTF play important roles in neuron survival, glial differentiation and brain tumor growth. However, the molecular mechanisms of CNTFRα regulation and its clinical significance in glioma remain largely unknown.

Fan et al. found CNTFRα was overexpressed in low-grade gliomas (LGG) compared with glioblastoma (GBM) and normal brain specimens in The Cancer Genome Atlas (TCGA) datasets and in an independent cohort. Bioinformatics analysis revealed a CpG shore of the CNTFRα gene regulated its mRNA expression in TCGA datasets. This observation was further validated with clinical specimens and functionally verified using demethylating agents. Additionally, we observed that independent of IDH mutation status, methylation of CNTFRα was significantly correlated with down-regulated CNTFRα gene expression and longer LGG patient survival. Interestingly, combination of CNTFRα methylation and IDH mutation significantly ($p < 0.05$) improved the prognostic prediction in LGG patients. Furthermore, the role of CNTFRα in glioma proliferation and apoptosis through the PI3K/AKT pathways was demonstrated by supplementation with exogenous CNTF in vitro and siRNA knockdown in vivo. Our study demonstrated that hypomethylation leading to CNTFRα up-regulation, together with autocrine expression of CNTF, was involved in glioma growth regulation. Importantly, DNA methylation of CNTFRα might serve as a potential epigenetic theranostic target for LGG patients [1].

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Fan K, Wang X, Zhang J, Ramos RI, Zhang H, Li C, Ye D, Kang J, Marzese DM, Hoon DSB, Hua W. Hypomethylation of CNTFRα is associated with proliferation and poor prognosis in lower grade gliomas. Sci Rep. 2017 Aug 1;7(1):7079. doi: 10.1038/s41598-017-07124-9. PubMed PMID: 28765641.